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Prenatal Development: Annotated Bibliography

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Prenatal Development

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Introduction

For decades, researchers have investigated how events in the prenatal period impact women and their infants. These studies, particularly by researchers in the medical, neuroscience, and behavioral science fields, led to discoveries of important information regarding the prenatal events that were strongly associated with mortality (or death) and morbidity (or incidences of injury, pathology and abnormalities/anomalies, and neurobehavioral sequelae) in the neonatal and infancy periods. Among the many common findings from early research studies, two are particularly noteworthy. First, maternal and fetal risk conditions arising in the prenatal period do not do so in isolation. Sameroff and Chandler characterized this as a “continuum of reproductive casualty,” in which several risks become linked together and affect events during pregnancy,

outcomes at birth, and in infant and child development in subsequent years (Sameroff, Arnold. J., and Michael J. Chandler. 1975. Reproductive risk and the continuum of caretaker casualty. In *Review of Child Development Research*. Vol. 4. Edited by Francis D. Horowitz, 187–244. Chicago: University of Chicago Press). Second, the impacts of these risk events on outcomes were found to vary, and not all pregnancies nor all neonates and infants were impacted to the same extent, if at all. Indeed, Sameroff and Chandler addressed the variability or uncertainty of impacts of prenatal events by adding a “continuum of caretaking casualty” to their model to include the important roles of family, society, and the environment. This resulting “transactional model of development” brought attention to the importance of genetic, biological, and environmental interactions before and after birth on the outcomes observed in neonates, infants, and children. Across time, research interests in prenatal and perinatal risks and their impacts on neonates, infants, and children have expanded to the extent that many variables heavily researched in the 1970s, 1980s, and 1990s are no longer hot topics. Instead, advances in research and meta-analysis designs, statistical and data modeling, new technologies, and multidisciplinary collaborations are enabling investigations that were either not attempted in the past or only to a limited extent.

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General Overviews

The framework for the publications included in this article is built from the writings of several authors whose works have important implications for understanding prenatal development and infant outcomes. These writings in particular have addressed the relation between gene-environment interactions, sometimes now framed as fetal programming, or the resetting of genetic programming during the fetal period due to environmental variables. There is evidence that fetal programming can change outcomes in the neonatal period and across the life span. While discussions of gene-environment interactions are not new, what is new are the efforts of researchers in different fields to understand whether and how genetic influences set trajectories for outcomes that may be moderated by environmental variables. Classic publications on genetic and environmental interactions include Waddington 1957, describing an “epigenetic landscape” depicting how the environment can influence the path of development set in motion by genes. Waddington’s theoretical and research contributions are well described by in the biography Slack 2002 and in McLearn 1970, in a chapter on genetics and behavioral development. From these publications we have a better understanding of the

application of fetal programming—an application to frame reconsiderations of preterm infant care, as described in Schug, et al. 2012; and a broader understanding of the continuum of prenatal development and infant outcomes, as presented in Hopkins and Johnson 2005. These publications, plus Sameroff and Chandler 1975, frame this article's focus on research investigations of fetal development, evidence of fetal programming, and the influence of prenatal events on infant outcomes, such as prenatal exposures to maternal drug use, mental health problems, obstetric events such as weight gain, and mother-infant attachment. Finally, there is a section on multivariate designs enabling investigations of the effects of moderating or mediating variables in studies of prenatal development and infant outcomes. Together, these publications reflect current pathways in research on prenatal development.

Hopkins, Brian, and Scott P. Johnson, eds. 2005. *Prenatal Development of Postnatal Functions*. Westport, CT: Praeger.

The seven chapters in this book focus on the continuity between prenatal events and postnatal outcomes. Chapters on the sensory and vestibular systems, brain structure and function, and the impacts of maternal anxiety and stress link theories and findings related to fetal programming, showing that early life events are detectable across the life span.

McLearn, Gearld. 1970. Genetic influences on behavior and development. In *Carmichael's manual of child psychology*. 3d ed. Edited by Paul H. Mussen, 39–76. New York: Wiley.

This chapter addresses behavior genetics and includes a description of Waddington's epigenetic landscape, complete with a graphic representation and examples from animal and human research. Although research citations are dated, there is a clear presentation on the basics of genetics, and behavior genetics intended to inform researchers focusing on human development.

Sameroff, Arnold J., and Michael J. Chandler. 1975. Reproductive risk and the continuum of caretaker casualty. In *Review of Child Development Research*. Vol. 4. Edited by Francis D. Horowitz, M. Hetherington, S. Scarr-Salapatek, and G. Siegel, 187– 244. Chicago: Univ. of Chicago Press.

This is a classic chapter focused on variables in the prenatal and perinatal periods that create risks for pregnancy outcomes and the development of neonates and infants. Research is reviewed on several reproductive risks and stressors as well as examples of research illustrating how caretaking casualty negatively impacts infant outcomes.

Schug, Thaddeus T., Adrian Erlebacher, Sarah Leibowitz, et al. 2012. Fetal programming and environmental exposures: Implications for prenatal care and preterm birth.

***Annals of the New York Academy of Sciences* 1276:37–46. DOI: 10.1111/nyas.12003**

The chapters herein present findings from multiple fields relevant to fetal programming through investigations of gene-gene and gene-environment interactions (or epigenetics) during the prenatal period. The conference goal is to use research findings to improve understanding of preterm birth and improve obstetric care. Available online for purchase or by subscription.

Slack, Jonathan M. W. 2002. Conrad Hal Waddington: The last Renaissance biologist? *Nature Reviews Genetics* 3:889–895. DOI: 10.1038/nrg933

This is a biography of the life and works of Conrad Waddington and with relevance to current research on the human genome. Details of Waddington's work preceding and succeeding the publication of *The Strategy of the Genes* that introduces the "epigenetic landscape" helps put Waddington's work into perspective. Available online for purchase or by subscription.

Waddington, Conrad H. 1957. *The Strategy of the Genes*. New York: Macmillan.

This classic work has complex but detailed descriptions of the epigenetic landscape. The pathways ("chreodes" or "creodes") and the paths ("canalization") of cell change are described along with mechanisms by which perturbations can occur. How genetic variation and environmental influences reach levels necessary for pathway changes are described.

Fetal Development

The articles in this section include research on fetal development specific to brain anatomy, the development of auditory and visual sensitivity, early indicators of temperament, learning and memory, and research evidence for and implications of fetal programming and epigenetics. Many of the studies reviewed, such as functional MRI (fMRI), magnetoencephalography, and diffusion tensor magnetic resonance imaging, are enabled by new or newer technologies and the use of combinations of techniques (behavioral, imaging, and genetic) to address issues of development as well as brain and behavior relations.

FETAL BRAIN ANATOMY

The focus here is on the development of fetal brain structures. Bystron, et al. 2008 updates previous research knowledge in a review of variables influencing the timing, sequencing, and complexity of developments in the cerebral cortex. Clowry, et al. 2010

reviews information on the neocortex, or the portion of the human brain that is uniquely human. Huang, et al. 2006 examines white and gray matter development using imaging techniques to study fetal, neonatal, and child brains, thus enabling an understanding of the developmental continuum of brain development. Huang, et al. 2012 reviews molecular genetic studies to discuss abnormalities in brain development. Joseph 2000 provides an overview of research findings on brain structure-function development. Prayer, et al. 2006 describes the use of in vivo MRIs for examining fetal brain structure and function. Marsh, et al. 2008 proposes the use of imaging techniques as viable methods for examining abnormal brain development in the context of psychiatric disorders in childhood.

Bystron, Irina, Colin Blakemore, and Pasko Rakic. 2008. Development of the human cerebral cortex: Boulder Committee revisited. *National Reviews Neuroscience* 9:110–122. DOI: 10.1038/nrn2252

A review article updating current knowledge about cerebral cortex development subsequent to the findings from the Boulder Committee report (1970). The focus is on the timing, sequence and complexity of events in development. Areas that were not known at the time of the Boulder Committee report, such as the subplate, are highlighted. Available online for purchase or by subscription.

Clowry, Gavin, Zoltan Molnár, and Pasko Rakic. 2010. Renewed focus on the developing human neocortex. *Journal of Anatomy* 217:276–288. DOI: 10.1111/j.1469-7580.2010.01281.x

This is a literature review examining the unique features of the human brain that set it apart from animal brains. These new studies are enabled by new methodological techniques.

Huang, Jin, Isabella Y. M. Wah, Ritsuko K. Pooh, and Kwong Wai Choy. 2012. Molecular genetics in fetal neurology. *Seminars in Fetal & Neonatal Medicine* 17:341–346. DOI: 10.1016/j.siny.2012.07.007

This review focuses on research from genetic studies to examine three common fetal neurological abnormalities related to disruptions in fetal brain development. The review uses genetic data to add to findings from magnetic imaging techniques on prenatal diagnoses. Available online for purchase or by subscription.

Huang, Hao, Jiangyang Zjang, Setsu Wakana, et al. 2006. White and gray matter development in human fetal, newborn and pediatric brains. *NeuroImage* 33:27–38. DOI: 10.1016/j.neuroimage.2006.06.009

In response to limited white matter growth studies, the authors use diffusion tensor

magnetic resonance imaging to examine postmortem fetal brains as well as neonate and child brains. Three-dimensional representations of the brains provide a glimpse at the development of white matter. Available online for purchase or by subscription.

Joseph, R. 2000. Fetal brain behavior and cognitive development. *Developmental Review* 20:81–98. DOI: 10.1006/drev.1999.0486

This is an overview of fetal brain development and its components throughout gestation. Functional links between developing brain areas and resulting neurobehavioral development, as well as fetal-neonate neurobehavioral characteristics, are discussed. Available online for purchase or by subscription.

Marsh, Rachel, Andrew J. Gerber, and Bradley S. Peterson. 2008. Neuroimaging studies of normal brain development and their relevance for understanding childhood neuropsychiatric disorders. *Journal of the American Academy of Child & Adolescent Psychiatry* 47.11: 1233–1251. DOI: 10.1097/CHI.0b013e318185e703

This article reviews the development of the prenatal and postnatal brain using imaging techniques, providing insight not only into normal brain development but also abnormal brain development that gives rise to psychiatric disorders in later life. Available online for purchase or by subscription.

Prayer, Daniela, Gregor Kasprian, Elisabeth Krampfl, et al. 2006. MRI of normal fetal brain development. *European Journal of Radiology* 57:199–216. DOI: 10.1016/j.ejrad.2005.11.020

This article reviews in vivo MRI findings of brain maturation rates of fetuses, beginning at 18 weeks gestational age, and describes anatomical, histological, and in vitro MRI data on progressions in structural development. Structure and function relations are described with reference to fetal movement. An excellent source of information on maturation of specific brain areas. Available online for purchase or by subscription.

FETAL SENSATION

Articles in this section examine the development of fetal visual and auditory systems. Well before birth, there is evidence that these systems are functional. While imaging technologies enable the inquiry in many of these studies, some studies use multiple methods. Eswaran, et al. 2004 employs magnetoencephalography (MEG) as a noninvasive tool for studying the fetal visual system. Fulford, et al. 2003 uses fMRI to study development of fetal visual and auditory systems, respectively, showing that these systems are functional before birth. Graven and Browne 2008a and Graven and Browne 2008b provide general overviews of research on structure and functional development of

the visual and auditory systems. Finally, Huotilainen 2010 describes “building blocks” of development in the fetal period that enable emotional and speech perception skills of the neonate.

Eswaran, Hari, Curtis L. Lowery, James D. Wilson, Pam Murphy, and Hubert Preissl. 2004. Functional development of the visual system in human fetus using magnetoencephalography. *Experimental Neurology* 19:S52–S58.

This article demonstrates the utility of MEG for studying human fetal brain development (28 weeks to term) by serially recording visual evoked responses to light flashes. Results of this study and the utility of MEG to monitor functional brain abnormalities are described. Available online for purchase or by subscription.

Fulford, Jonathan, Shantala H. Vadeyar, Senani H. Dodampahala, et al. 2003. Fetal brain activity in response to a visual stimulus. *Human Brain Mapping* 20:239–245. DOI: 10.1002/hbm.10139

This study compared fetal and adult fMRI responses to an auditory stimulus. Seven of eighteen fetal responses and five of thirteen adult responses were localized in the temporal region. Fetal responses show no average time to peak differences from adults. Differences in time course of hemodynamic responses are found. Implications for detecting pregnancy abnormalities are noted. Available online for purchase or by subscription.

Graven, Stanley N., and Joy V. Browne. 2008a. Auditory development in the fetus and infant. *Newborn and Infant Nursing Reviews* 8.4: 187–193. DOI: 10.1053/j.nainr.2008.10.010

Auditory development of the fetus and infant is reviewed, particularly the structure of the auditory system and the factors involved in auditory development. The implications of fetal and neonatal sound exposure for system development and the mother-infant attachment process are described. Available online for purchase or by subscription.

Graven, Stanley N., and Joy V. Browne. 2008b. Visual development in the human fetus, infant, and young child. *Newborn and Infant Nursing Reviews* 8.4: 194–201. DOI: 10.1053/j.nainr.2008.10.011

Visual development of the fetus and infant is reviewed, particularly prenatal and postnatal structural development, as well as the factors influencing development. The impacts of prenatal and postnatal sleep deprivation/disruption and rapid eye movement for visual development are described. Available online for purchase or by subscription.

Huotilainen, M. 2010. Building blocks of fetal cognition: Emotion and language. *Infant and Child Development* 19:94–98. DOI: 10.1002/icd.658

This review article discusses research findings on the fetal precursors to the auditory and visual skills that are shown by the neonate. Some information on emotional and speech perception skills of the neonate are described along with suggestions for detection of developmental delays. Available online for purchase or by subscription.

FETAL TEMPERAMENT

Although biologically based, temperament is also a product of early environment and experience. Evaluations of temperament in infancy are often based on parent perceptions, but researchers have expanded temperament data sources using biological and behavioral indicators from the prenatal period. These studies highlight pre- and postnatal factors, such as maternal stress, fetal heart rate and movement, and parent emotion, related to measures of infant temperament. DiPietro, et al. 1996 examines antecedents of “aversive” and “less aversive” infant temperament traits using data from the fetal period, while DiPietro, et al. 2003 examines stability of state regulation from the fetal to infancy periods. Eaton and Saudino 1992 reports that fetal movement meets established criteria for defining temperament. Werner, et al. 2007 examines infant temperamental reactivity as predictors of temperament from fetal and postnatal measures.

DiPietro, Janet A., Kathleen A. Costigan, and Eva K. Pressman. 2003. Fetal state concordance predicts infant state regulation. *Early Human Development* 68:1–13. DOI: 10.1016/S0378-3782(02)00006-3

This is an empirical study examining fetal state regulation based on fetal heart rate and movement for effects on neonatal state regulation to determine the stability of state regulation. Fetal regulation at 36 weeks and infant state regulation were related. Available online for purchase or by subscription.

DiPietro, Janet A., Denise M. Hodgson, Kathleen A. Costigan, and Timothy R. B. Johnson. 1996. Fetal antecedents of infant temperament. *Child Development* 67.5: 2568–2583. DOI: 10.2307/1131641

An empirical study of infant temperament as predicted by measures of fetal heart rate and movement. More aversive traits (e.g., more difficult, less adaptable, unpredictable) were related to higher in utero activity, and less aversive traits (e.g., less activity, more predictability) were related to higher heart rates in utero. Findings support temperament as biologically based and evident early. Available online for

purchase or by subscription.

Eaton, Warren O., and Kimberly J. Saudino 1992. Prenatal activity level as a temperament dimension? Individual differences and developmental functions in fetal movement. *Infant Behavior and Development* 15.1: 57–70. DOI: 10.1016/0163-6383(92)90006-R

Fetal activity was evaluated as an indicator of temperament and met criteria of “present early in life, reflecting behavioral tendencies, constitutional foundation, and showing continuity across time.” Links to postnatal temperament were not investigated. Available online for purchase or by subscription.

Werner, Elizabeth A., Michael M. Myers, William P. Fifer, et al. 2007. Prenatal predictors of infant temperament. *Developmental Psychobiology* 49.5: 474–484. DOI: 10.1002/dev.20232

Fetal heart rate and maternal postnatal psychiatric illness were assessed for 50 mother-infant dyads. Both measures were associated with infant reactivity after controlling for maternal postnatal anxiety levels. Findings suggest that temperament is identifiable before birth, and intrauterine factors may contribute to infant temperament. Available online for purchase or by subscription.

FETAL LEARNING AND MEMORY

Studies of fetal learning and memory included in this section use discrimination, habituation, and learning paradigms. Dirix, et al. 2009 provides evidence of fetal learning and memory at 30 weeks gestation and notes changes in memory and recall evident at 34 weeks. Gonzalez-Gonzalez, et al. 2006 and Granier-Deferre, et al. 2011 use auditory stimuli to demonstrate that prenatal exposure to repeated stimuli is related to recognition of similar stimuli after birth. James 2010 reviews studies of fetal habituation and learning and questions the implications of these studies for postnatal life. Kisilevsky and Hains 2010 review studies investigating the reliability of fetal heart rate as an indicator of fetal discrimination, habituation, and learning. Morokuma, et al. 2008 shows that fetuses less than 35 weeks gestational age do not show consistent habituation to low-intensity sounds, but those over 35 weeks do.

Dirix, Chantal E. H., Jan G. Nijhuis, Henk W. Jongsma, and Gerard Hornstra. 2009. Aspects of fetal learning and memory. *Child Development* 80.4: 1251–1258. DOI: 10.1111/j.1467-8624.2009.01329.x

Fetal learning was assessed using habituation of fetal movement to an auditory stimulus. Fetuses demonstrated learning at 30 to 34 weeks gestation and by 34 weeks

gestation can store and retrieve information across a 4-week period. Relation of learning to gestational age is described.

Gonzalez-Gonzalez, N. L., M. N. Suarez, B. Perez-Piñero, H. Armas, E. Domenech, and J. L. Bartha. 2006. Persistence of fetal memory into neonatal life. *Acta Obstetricia et Gynecologica* 85:1160–1164. DOI: 10.1080/00016340600855854

This is an empirical study demonstrating the persistence of fetal auditory memory into the newborn period. Neonates prenatally exposed to an auditory stimulus habituated faster than control neonates without prenatal auditory stimulus exposure. These findings support the presence of learning and memory in fetuses that persist after birth. Available online for purchase or by subscription.

Granier-Deferre, Carolyn, Sophie Bassereau, Aurelie Ribeiro, Anne-Yvonne Jacquet, and Anthony J. DeCasper. 2011. A melodic contour repeatedly experienced by human near-term fetuses elicits a profound cardiac reaction one month after birth. *PLoS ONE* 6.2: e17304.

This study extends evidence of prenatal learning and memory at birth to one month after birth. Infants prenatally exposed to a melody had larger heart rate deceleration when exposed to a similar melody as compared to infants never prenatally exposed. Implications of the findings for the perceptual tuning of the auditory system are discussed.

James, David. K. 2010. Fetal learning: A critical review. *Infant and Child Development* 19:45–54. DOI: 10.1002/icd.653

The article reviews research involving fetal habituation and learning. Definitions of learning, methods for studying and measuring fetal learning, as well as findings and limitations of the studies reviewed are described. The relation of fetal learning to child development is questioned. Available online for purchase or by subscription.

Kisilevsky, Barbara S., and Sylvia M. J. Hains. 2010. Exploring the relationship between fetal heart rate and cognition. *Infant and Child Development* 19.1: 60–75. DOI: 10.1002/icd.655

This review examines the role in fetal heart rate measures in studies of discrimination, habituation, and auditory learning. Issues related to HR (methodology, maturation, neural regulation, and links to cognition) are described. Clear evidence from classic and recent studies of prenatal cognitive skills is presented. Available online for purchase or by subscription.

Morokuma, Seiichi, Valentina Doria, Antonio Ierullo, et al. 2008. Developmental change in fetal response to repeated lowintensity sound. *Developmental Science* 11.1: 47–52. DOI: 10.1111/j.1467-7687.2007.00646.x

Developmental differences in fetal habituation to auditory stimuli are examined in this study. Fetuses at 35 to 37 weeks exhibit rapid heart rate habituation, whereas those 32 to 34 weeks show variable responses and little recovery to a new stimulus. The findings align with other researchers' findings that fetuses habituate to auditory stimulus. Available online for purchase or by subscription.

FETAL PROGRAMMING

There is strong interest in understanding how events in the prenatal period may influence the course of fetal and infant development. In this section, psychological, cognitive, health, and social outcomes are considered from the view of fetal programming. Barker 2002 discusses the relation between coronary heart disease in later life and growth in utero and in childhood. Ellison 2010 discusses epigenetics and fetal programming in the context of physical and mental health. Gluckman and Hanson 2010 proposes that fetal programming is adaptive, but maladaptive consequences can arise. The placenta, carrying nutrients from mother to fetus, plays a role in fetal programming as described in Godfrey 2002. Kaiser and Sachser 2009 uses results of animal studies to argue for an adaptive view of stress exposure. Mathers and McKay 2009 points to maternal diet and impacts on DNA expression, and describes the relations between epigenetics and fetal programming. Poggi, et al. 2012 examines how prenatal exposure to maternal stress might program stress responses in infancy. Shlotz and Phillips 2009 discusses the fetal origins of mental health disorders and prenatal risk conditions.

Barker, David J. P. 2002. Fetal programming of coronary heart disease. *Trends in Endocrinology & Metabolism* 13.9: 364–368. DOI: 10.1016/S1043-2760(02)00689-6

This is an empirical study of men and women who developed or died from coronary heart disease, size at birth and infancy, and gains in weight and body mass index in childhood. For both genders, small birth and infancy size, and rapid gains in childhood characterize risk for coronary heart disease. Mechanisms related to these findings are discussed. Available online for purchase or by subscription.

Ellison, Peter T. 2010. Fetal programming and fetal psychology. *Infant and Child Development* 19.1: 6–20. DOI: 10.1002/icd.649

This article reviews the fetal programming hypothesis and implications for public health, such as impacts of specific perinatal risks on physical and mental health. The authors address how this hypothesis might reflect an updated theory of evolution when

considering epigenetic patterns. Evidence from human and animal studies is discussed. Available online for purchase or by subscription.

Gluckman, Peter D., and Mark A. Hanson. 2010. The plastic human. *Infant and Child Development* 19:21–26. DOI: 10.1002/icd.650

The authors discuss fetal programming as developmental plasticity. Such plasticity can originate as “adaptive” but “maladaptive consequences” arise from interactions between genes and environment. Birth weight has been discussed as a biological marker for maladaptive consequences, but a broader consideration of early biological markers is needed to understand phenotypic variations. Available online for purchase or by subscription.

Godfrey, Keith M. 2002. The role of the placenta in fetal programming: A review. *Placenta* 23:S20–S27.

This review examines fetal programming as affected by maternal factors during pregnancy, placental functioning, and fetal development. Placenta functioning is discussed as a focus for intervention that can impact the long-term health of the infant. Available online for purchase or by subscription.

Kaiser, Sylvia, and Norbert Sachser. 2009. Effects of prenatal social stress on offspring development: Pathology or adaptation? *Current Directions in Psychological Science (Wiley-Blackwell)* 18:118–121. DOI: 10.1111/j.1467-8721.2009.01620.x

This review of animal studies examines the influences of prenatal exposure to environmental stress. Rather than being pathological, the authors argue that stress exposure preadapts the fetus to the postnatal environment. Social stability and instability as related to fetal adaptation are discussed. Available online for purchase or by subscription.

Mathers, John C., and Jill A. McKay. 2009. Epigenetics—potential contribution to fetal programming. *Advances in Experimental Medicine And Biology* 646:119–123. DOI: 10.1007/978-1-4020-9173-5_13

The authors discuss evidence of the impact of maternal diet on DNA methylation and modification of histones of the developing fetus. Epigenetic changes are implicated in fetal programming and in understanding the developmental origins of health. Epigenetic changes occurring in later life are also discussed. Available online for purchase or by subscription.

Poggi Davis, Elysia, Laura M. Glynn, Feizal Waffarn, and Curt A. Sandman. 2012. Prenatal maternal stress programs infant stress regulation. *Journal of Child Psychology And*

Psychiatry 52.2: 119–129. DOI: 10.1111/j.1469-7610.2010.02314.x

This empirical study investigates prenatal maternal cortisol and maternal psychosocial stress as possible fetal programming sources of infant responses to stress. Exposure to maternal stress in the last two trimesters was related to higher measures of cortisol and slower behavioral recovery in infants based on a heel-stick procedure. Available online for purchase or by subscription.

Shlotz, Wolff, and David I. W. Phillips. 2009. Fetal origins of mental health: Evidence and mechanisms. *Brain, Behavior, and Immunity* 23.7: 905–916. DOI: 10.1016/j.bbi.2009.02.001

The authors review studies linking personality disorders and risk of psychopathology to fetal programming. A variety of maternal prenatal, parental genetic, and fetal environment factors are modeled as relating to mental health outcomes. Implications for future research and opportunities for interventions are discussed. Available online for purchase or by subscription.

Prenatal Exposures

Research in this section examines the impacts of prenatal exposures to a variety of fetal stressors, such as nicotine, alcohol, legal and illegal drugs, as well as poly-drug use, and to maternal mental health conditions. Reviewed studies examine impacts of these fetal stressors using a variety of outcomes measured in the neonatal and infancy periods as well as at other ages across the life span. Complex issues of exposure timing (trimester), methods of exposure verification and dosage/severity, and how the presence of other explanatory factors are addressed are all touched on in articles across sections. Research findings show that infant outcomes differ across timing of exposure and type of exposure. Researchers discuss the need for considering additional factors in understanding links between prenatal exposures and infant outcomes.

EXPOSURE TO NICOTINE

Exposure to smoking in utero has been linked to negative infant outcomes, most notably low birth weight, impaired fetal growth, and preterm birth. Recent research provides evidence of links between prenatal smoking and cognitive and/or behavioral outcomes. Bernstein, et al. 2005 and Roza, et al. 2007 explore the effects of timing of fetal nicotine exposure and fetal and infant birth weight or head growth. Cornelius and Day 2009 reviews behavioral, genetic, and imaging studies of nicotine exposure at several gestational ages. Ernst, et al. 2001 includes reviews of human and animal studies on

consequences of prenatal nicotine exposure. Fenercioglu, et al. 2009, Król, et al. 2012, and Samper, et al. 2012 use somewhat different methods to compare impacts of active, passive, and nonsmoking on measures of newborn and infant growth. Webhy, et al. 2011 includes consideration of socio-economic status (SES) in investigating the impacts of maternal smoking on infant neurobehavioral development.

Bernstein, Ira M., A. Mongeon Joan, Gary J. Badger, Laura Solomon, Sarah H. Heil, and Stephen T. Higgins. 2005. Maternal smoking and its association with birth weight. *Obstetrics Gynecology* 106.5, Part 1: 986–991. DOI: 10.1097/01.AOG.0000182580.78402.d2

Mothers' patterns of smoking by trimester were examined to determine the relationship to infant birth weight. Smoking during the third trimester was associated with lower birth weight. Effects at the per-cigarette level in the third trimester and effects on birth weight are presented.

Cornelius, Marie D., and Nancy L. Day. 2009. Developmental consequences of prenatal tobacco exposure. *Current Opinion in Neurology* 22.2: 121–125. DOI: 10.1097/WCO.0b013e328326f6dc

This is a review of human research (2007–2008) focusing largely on prospective studies with biologically verified tobacco exposure. Evidence is presented on infant through adolescent samples (including contrary findings) from behavioral, genetic, and some imaging methodologies. Each article is reviewed, and reviewed sections are very brief. Available online for purchase or by subscription.

Ernst, Monique, Eric T. Moolchan, and Miquen L. Robinson. 2001. Behavioral and neural consequences of prenatal exposure to nicotine. *Journal of the American Academy of Child and Adolescent Psychiatry* 40.6: 630–641. DOI: 10.1097/00004583-200106000-00007

The article reviews human and animal research on prenatal nicotine exposure and prenatal, perinatal, and postnatal outcomes. Human studies include evidence of effects on neurobehavioral outcomes (infancy to adulthood). Animal studies include evidence of impacts, in utero and postnatal, and evidence of impacts on neural mechanisms. Available online for purchase or by subscription.

Fenercioglu, A. K., I. Tamer, G. Karatekin, and A. Nuhoglu. 2009. Impaired postnatal growth of infants prenatally exposed to cigarette smoking. *Tohoku Journal of Experimental Medicine* 218.3: 221–228. DOI: 10.1620/tjem.218.221

Maternal smoking, passive smoking, and nonsmoking were examined in relation to head circumference, weight, and height at birth, 3 months, and 6 months. Deficits in

growth on the three measures were found at 6 months for infants of smokers, but infants of passive smokers had caught up. Available online for purchase or by subscription.

Król, Marzenna, Ewa Florek, Wojciech Piekoszewski, Renata Bokiniec, and Maria K. Kornacka. 2012. The influence of prenatal exposure to tobacco smoke on neonatal body proportions. *Journal of Women's Health Care* 1:117. DOI: 10.4172/2167-0420.1000117

This empirical study examines neonatal anthropometric outcomes (weight, crown-heel length, head and chest circumference, ponderal index [relation of weight to length]) and maternal active/passive smoking and nonsmoking. Impacts of active smoking were found for all outcomes except ponderal index; passive smoking effects on outcomes were not significant.

Roza, Sabine J., Bero Verburg, Vincent W. V. Jaddoe, et al. 2007. Effects of maternal smoking in pregnancy on prenatal brain development. The generation R study. *European Journal of Neuroscience* 25.3: 611–617. DOI: 10.1111/j.1460-9568.2007.05393.x

This prospective study of maternal smoking in early, mid-, and late pregnancy uses questionnaires and measures of head and brain growth. Prenatal smoking reduced head and brain growth. Three mechanisms to explain links of smoking in pregnancy and neurobehavioral development of the fetus and infant are discussed. Available online for purchase or by subscription.

Samper, M. P., A. Jiménez-Muro, I. Nerín, A. Marqueta, P. Ventura, and G. Rodríguez. 2012. Maternal active smoking and newborn body composition. *Early Human Development* 88.3: 141–145. DOI: 10.1016/j.earlhumdev.2011.07.015

This empirical study examines effects of exposure to maternal smoking and body composition. While all measures of infant body composition were heavier for nonsmoking than smoking mothers, no differences were found for the ponderal index. Infants prenatally exposed to smoke had leaner body mass, lower body fat, and lower birth weights. Available online for purchase or by subscription.

Webhy, George L., Kaitlin Prater, Ann Marie McCarthy, Eduardo E. Castilla, and Jeffrey C. Murray. 2011. The impact of maternal smoking during pregnancy on early child neurodevelopment. *Journal of Human Capital* 5.2: 207–254. DOI: 10.1086/660885

This is a prospective study of maternal smoking in pregnancy, SES, and neurobehavioral outcomes in South American infants (3 and 24 months). Neurobehavioral outcomes were poorer in the smoking group, with increased negative neurodevelopmental outcomes in the low SES sample. Smoking rates were higher in the low SES compared

to high SES sample. Available online for purchase or by subscription.

EXPOSURE TO ALCOHOL

Articles in this section address evidence of the consequences of prenatal exposure to alcohol. Consistent across studies are findings that negative outcomes are dependent upon dosage and timing of exposure to alcohol. Chen 2012 finds relations between alcohol use during pregnancy and infant temperament, and to a lesser extent on birth weight; Haley, et al. 2006 reports impacts on infant stress reactions from fetal alcohol exposure. Hannigan and Armant 2000 provides descriptions of diagnostic criteria used in studies of prenatal alcohol exposure and reviews evidence of impacts on a variety of outcomes. Henderson, et al. 2007 reviews outcomes from exposure to low-to-moderate alcohol use. Testa, et al. 2003 describes results of a meta-analysis showing that alcohol exposure impacted infant outcomes only in a narrow age range.

Chen, Jen-Hao. 2012. Maternal alcohol use during pregnancy, birth weight, and early behavioral outcomes. *Alcohol and Alcoholism* 47.6: 649–656. DOI: 10.1093/alcalc/ags089

This study examined a national dataset for effects of maternal alcohol use during pregnancy on infant behavior, temperament, and birth weight. Models tested were adjusted for some confounds. Prenatal alcohol use had less impact on birth weight compared to temperament, with effects found for temperamental “difficultness” even when use was low-to-moderate. Available online for purchase or by subscription.

Haley, David W., Nancy S. Handmaker, and Jean Lowe. 2006. Infant stress reactivity and prenatal alcohol exposure. *Alcoholism: Clinical and Experimental Research* 30.12: 2055–2064. DOI: 10.1111/j.1530-0277.2006.00251.x

This study examined the effect of prenatal alcohol exposure on emotion and stress regulation measured by cortisol level, heart rate, and behavior in 5- to 7-month olds. Impacts on all emotion and stress measures were found, along with some gender effects. Controls for maternal depression and income did not alter results. Available online for purchase or by subscription.

Hannigan, John H., and D. Randall Armant. 2000. Alcohol in pregnancy and neonatal outcome. *Seminars in Neonatology* 5:243–254. DOI: 10.1053/siny.2000.0027

This review targets prenatal alcohol consumption and its impacts on the fetus and newborn. Diagnostic criteria for fetal alcohol syndrome (FAS) and alcohol-related neurodevelopmental disorder (ARND) are described, along with information on outcomes (e.g., spontaneous abortion, gestation length, birth weight, facial

dysmorphology, and other selected birth defects). FAS and ARND are evident in the newborn. Available online for purchase or by subscription.

Henderson, J., R. Gray, and P. Brocklehurst. 2007. Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. *International Journal of Obstetrics and Gynecology* 114:243–252. DOI: 10.1111/j.1471-0528.2006.01163.x

This article is a systematic review of 46 studies of the impacts of low-to-moderate alcohol consumption in pregnancy. No consistent effects are reported for selected outcomes (stillbirth, impaired growth, birth weight, preterm birth, and physical malformations). Methodological weaknesses in reviewed studies are noted. Tables summarizing reviewed studies are provided.

Testa, Maria, Brian M. Quigley, and Rina Das Eiden. 2003. The effects of prenatal alcohol exposure on infant mental development: A meta-analytical review. *Alcohol and Alcoholism* 38.4: 295–304. DOI: 10.1093/alcalc/agg087

This meta-analysis includes 10 studies examining the effects of prenatal alcohol exposure on infant mental development at 6–8, 12–13, and 18–24 months. Alcohol exposure had negative effects on mental development at 12–13 months only. Impacts were related to dosage level. Possible reasons for inconsistencies across age groups are discussed.

EXPOSURE TO ANTIPSYCHOTIC AND PSYCHOTROPIC DRUGS

The articles in this section explore relations between negative infant outcomes and use of antipsychotic and psychotropic medications in pregnancy, with the caveat that disentangling mental health and drug use is difficult. Emory and Dieter 2006 reports the results of three studies indexing fetal sensitivity to maternal depression and psychotropic drug use. Gentile 2010 identifies methodological difficulties in the consistency of findings across forty-one studies involving psychotropic drug exposure. Johnson, et al. 2012 differentiates impacts of antipsychotic and psychotropic drugs on infant outcomes. Oberlander, et al. 2006 separates antidepressant drug use and nonuse in depressed mothers to study impacts of newborn outcomes. Weikum, et al. 2012 links fetal and infant auditory discrimination with maternal depression and use of antidepressants.

Emory, Eugene K., and John N. I. Dieter. 2006. Maternal depression and psychotropic medication effects on the human fetus. *Annals of the New York Academy of Sciences* 1094.1: 287–291. DOI: 10.1196/annals.1376.036

Three studies examined: 1) fetal activity of depressed mothers across gestation; 2) effects of maternal depression and anxiety on responsivity in late term fetuses; and 3) effects of psychotropic medication on fetal cerebral blood flow. Findings show evidence of

fetal sensitivity to maternal mental state and use of psychotropic medication. Available online for purchase or by subscription.

Gentile, Salvatore. 2010. Neurodevelopmental effects of prenatal exposure to psychotropic medications. *Depression and Anxiety* 27:675–686. DOI: 10.1002/da.20706

This is a review of forty-one studies on the effects of prenatal exposure to psychotropic medications and infant mental development. Separate tables are presented with results for each medication considered. Some consistencies in results are noted. Difficulty in finding consistent results with some medications is attributed to varying dosages and timing of exposure in utero. Available online for purchase or by subscription.

Johnson, Katrina C., Jamie L. LaPrarie, Patricia Brennan, Zachary Stowe, and Jeffrey Newport. 2012. Prenatal antipsychotic exposure and neuromotor performance during infancy. *Archives of General Psychiatry* 69.8: 787–794. DOI: 10.1001/archgenpsychiatry.2012.160

This is a prospective study of prenatal exposure to antipsychotic, antidepressant, or no medication and neuromotor performance and habituation in 6-month-old infants. Antipsychotic (but not antidepressant exposure) impacted infant neuromotor performance. Performance was related to maternal psychiatric history. No effect on habituation was observed. Available online for purchase or by subscription.

Oberlander, Tim F., William Warburton, Shaila Misri, Jaafar Aghajanian, and Clyde Hertzman. 2006. Neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitor antidepressants and maternal depression using population-based linked health data. *Archives of General Psychiatry* 63:898–906. DOI: 10.1001/archpsyc.63.8.898

A population database is used to study prenatal exposure to antidepressants and maternal depression on newborn outcomes compared with those of mothers with depression but not medication exposed. Exposed infants had lower birth weights and higher incidence of respiratory distress, jaundice, and feeding problems. Propensity matching controlled for mental illness severity.

Weikum, Whitney M., Tim F. Oberlander, Takao K. Hensch, and Janet F. Werker. 2012. Prenatal exposure to antidepressants and depressed maternal mood alter trajectory of infant speech perception. *Proceedings of the National Academy of Sciences of the United States of America* 109:17221–17227. DOI: 10.1073/pnas.1121263109

This empirical study examined the impacts of exposure to antidepressants (serotonin reuptake inhibitors, or SRIs) during pregnancy on fetal consonant and vowel discrimination and infant

speech and language discrimination. Maternal prenatal depression and using SRIs during pregnancy affect development of speech perception skills.

EXPOSURE TO ILLEGAL DRUGS

The use of illicit drugs during pregnancy is difficult to research due to many factors including legal implications. However, the articles in this section provide evidence that prenatal exposure to cocaine, marijuana, and methamphetamine does have some, but often differential, impacts on infant outcomes. Behnke, et al. 2013 reports on prevalence, mechanisms, and detection of prenatal exposure to common illegal drugs and infant outcomes. Frank, et al. 2002 reports that prenatal cocaine exposure is related to infant outcomes but impacts can be modified by caretaking and birth weight variables. Fried and Smith 2001 reviews the literature on prenatal marijuana exposure and infant and child executive function skills, as well as the issues that complicate conclusions from drug exposure studies. Jutras-Aswad, et al. 2009 reviews possible mechanisms by which exposure impacts brain development. Singer, et al. 2002 reports impacts of prenatal cocaine exposure on mental development of infants and toddlers, and Smith, et al. 2011 reports impacts of methamphetamine exposure on infant motor development.

Behnke, Marylou, and Vincent C. Smith 2013. Prenatal substance abuse: Short- and long-term effects on the exposed fetus. *Pediatrics* 131.3: e1009–e1024. DOI: 10.1542/peds.2012-3931

A technical report presenting findings on prevalence of common illegal drug in prenatal exposures, methods of exposure identification, mechanisms of action in fetal development, and short- and long-term outcomes of exposed infants.

Frank, Deborah A., Ruth Rose Jacobs, Marjorie Beeghly, et al. 2002. Level of prenatal cocaine exposure and scores on the Bayley Scales of Infant Development: Modifying effects of caregiver, early intervention, and birth weight. *Pediatrics* 110.6: 1143–1152. DOI: 10.1542/peds.110.6.1143

This is a prospective longitudinal study of differential prenatal cocaine exposures on infant development at 6, 12, and 24 months. Cocaine dosage from maternal report assays did not affect measured outcomes, but cocaine exposure, gestational age, low birth weight, and kinship care were related to developmental scores. Available online for purchase or by subscription.

Fried, Peter A., and A. M. Smith. 2001. A literature review of the consequences of prenatal marijuana exposure: An emerging theme of a deficiency in aspects of executive function. *Neurotoxicology and Teratology* 23:1–11. DOI: 10.1016/S0892-

0362(00)00119-7

This is a review of the literature examining effects of prenatal marijuana exposure on outcomes (IQ, executive function, brain structure and function, neurobehavioral, and cognitive abilities) from newborn to school-age children. Issues that complicate the interpretation of results of empirical studies are reviewed. Available online for purchase or by subscription.

Jutras-Aswad, Didier, Jennifer A. DiNieri, Tibor Harkany, and Yasmin L. Hurd. 2009. Neurobiological consequences of maternal cannabis on human fetal development and its neuropsychiatric outcome. *European Archives of Psychiatry and Clinical Neuroscience* 259:395–412. DOI: 10.1007/s00406-009-0027-z

This literature review examines the effect of prenatal marijuana exposure on fetal brain development, infant behaviors, cognitive abilities, and subsequent neuropsychiatric disorders. Mechanisms by which marijuana exposure may influence later outcomes due to its effect on neurotransmitters are described with supporting research evidence. Available online for purchase or by subscription.

Singer, Lynn T., Robert Arendt, Sonia Minnes, et al. 2002. Cognitive and motor outcomes of cocaine-exposed infants. *Journal of the American Medical Association* 287.15: 1952–1960. DOI: 10.1001/jama.287.15.1952

This prospective, longitudinal study examines high-risk, low SES, prenatal, cocaine exposed infant at 6.5, 12, and 24 months of age. Cocaine exposure significantly depressed mental development performance at 2 years old. No effects of cocaine exposure on motor development were found. Discussion of study limitations and conclusions is detailed.

Smith, Lynne M., Linda L. LaGasse, Chris Derauf, et al. 2011. Motor and cognitive outcomes through three years of age in children exposed to prenatal methamphetamine. *Neurotoxicology and Teratology* 33.1: 176–184. DOI: 10.1016/j.ntt.2010.10.004

This prospective study examines prenatal methamphetamine exposure on motor and cognitive skills of children at 1–3 years of age. Multiple controls for covariates were used. Methamphetamine exposure impacted fine motor skills at age 1, but not age 3. No effects on cognitive development were found. The need for follow-ups beyond 3 years is discussed. Available online for purchase or by subscription.

POLYDRUG EXPOSURE

One difficulty in conducting research on impacts of prenatal drug exposure is that drug

use often involves more than one drug. Thus, it is difficult to attribute specific outcomes to specific drugs. The articles in this section examine the effects of polydrug exposure in utero. Asanbe, et al. 2006 reports that children prenatally exposed to cocaine and/or polydrugs differed from matched controls on some but not all cognitive measures. Noland, et al. 2003 investigates impacts of cocaine and polydrug exposure on executive function skills of infants. Singer, et al. 2012 investigates use of Ecstasy and polydrug use during pregnancy and outcomes for the women and for their infants. Smith, et al. 2006 examines prenatal Ecstasy and polydrug exposure and SES on fetal growth. Thompson, et al. 2009 reviews the results of animal studies for evidence of drug exposure impacts on brain development.

Asanbe, Comfort B., and Edna Lockert. 2006. Cognitive abilities of African American children with prenatal cocaine/polydrug exposure. *Journal of Health Care for the Poor and Underserved* 17.2: 400–412. DOI: 10.1353/hpu.2006.0054

Prenatal cocaine/polydrug exposed and nonexposed African American children ages 6 and 8 years were studied. Compared to matched controls, IQ differences, but not differences in distractibility tasks, were identified. Interpretations of findings question generalizations about cocaine exposure and child outcomes. Available online by subscription.

Noland, Julia S., Lynn T. Singer, Sudhir K. Mehta, and Dennis Super. 2003. Prenatal cocaine/polydrug exposure and infant performance on an executive functioning task. *Developmental Neuropsychology* 24.1: 499–517. DOI: 10.1207/S15326942DN2401_05

An investigation of level of exposure to cocaine and/or polydrugs prenatally and 9- to 12-month-old infants' working memory, inhibitory control, and planning assessed by A-not-B task performance. Effects of heavy exposure remained even after an array of possible confounding variables and mediators were analyzed. Available online for purchase or by subscription.

Singer, Lynn T., Derek G. Moore, Sarah Fulton, et al. 2012. Neurobehavioral outcomes of infants exposed to MDMA (Ecstasy) and other recreational drugs during pregnancy. *Neurotoxicology and Teratology* 34.3: 303–310. DOI: 10.1016/j.ntt.2012.02.001

This prospective study examines exposure to MDMA in the prenatal period in polydrug using women and neonatal and infant outcomes. MDMA exposure did not yield differences in neurobehavioral outcomes at 1 month or differences on cognitive measures at 4 months. Differences in motor performance were found at 4 months. Maternal consequences of MDMA use are described. Available online for purchase or by subscription.

Smith, Lynne M., Linda L. LaGasse, Chris Derauf, et al. 2006. The infant development, environment, and lifestyle study: Effects of prenatal methamphetamine exposure, polydrug exposure, and poverty on intrauterine growth. *Pediatrics* 118.3: 1149–1156. DOI: 10.1542/peds.2005-2564

This prospective study investigates prenatal MDMA exposure and fetal growth. MDMA exposed infants were more likely to be small for gestational age and have lower birth weight, after adjusting for covariates (smoking, alcohol, marijuana) than nonexposed infants. The developmental sequelae of small for gestational age and low birth weight are discussed. Available online for purchase or by subscription.

Thompson, Barbara L., Pat Levitt, and Gregg D. Stanwood. 2009. Prenatal exposure to drugs: Effects on brain development and implications for policy and education. *National Review of Neuroscience* 10.4: 303–312. DOI: 10.1038/nrn2598

This review article includes evidence from animal models to examine the effect of prenatal drug exposure, including cocaine, methamphetamine, nicotine, alcohol, antidepressants, and other prescription medications on brain development. Future directions for research studies and implications of findings for policymakers are described. Available online for purchase or by subscription.

EXPOSURE TO MATERNAL DEPRESSION AND ANXIETY

Maternal depression and anxiety may arise due to biological changes (i.e., hormonal), environmental effects (i.e., domestic violence, medical problems) during pregnancy, or idiopathically. Davalos, et al. 2012; Field 2011; Pearson, et al. 2012; and Van Batenburg-Eddes, et al. 2009 each target prenatal and postnatal influences from maternal anxiety and/or depression to investigate impacts on fetal, infant, and/or child development and mother-infant interactions. There are methodological differences across studies. While postnatal anxiety and/or depression are studied most often, these authors argue for the importance of studying mental health conditions during pregnancy. Brouwers, et al. 2001 investigates how timing of prenatal exposure to maternal anxiety impacts infant development. Kinsella and Monk 2009 uses a fetal programming view to integrate findings in their literature review on effects of maternal mental health across the life-span. Wojcicki, et al. 2011 finds that Latino infants grew at a slower rate when exposed pre- and postnatally to maternal depression.

Brouwers, Evelien, Anneloes L. van Barr, and Victor J. M. Pop. 2001. Maternal anxiety during pregnancy and subsequent infant development. *Infant Behavior and Development* 24:95–106. DOI: 10.1016/S0163-6383(01)00062-5

This prospective study investigates the influence of prenatal maternal anxiety on infant and child outcomes. Timing of exposure, particularly in late pregnancy, influenced outcomes. Explanations of these findings using the current study and results of other studies are provided. Available online for purchase or by subscription.

Davalos, Deana B., Carly A. Yadon, and Hope C. Tegellas. 2012. Untreated prenatal maternal depression and the potential risks to offspring: A review. *Archives of Women's Mental Health* 15:1–14. DOI: 10.1007/s00737-011-0251-1

This review article examines the influence of unmedicated maternal prenatal depression and infant outcomes. The authors argue that prenatal depression is understudied compared to postpartum depression. A detailed table summarizing the reviewed literature is provided. Available online for purchase or by subscription.

Field, Tiffany. 2011. Prenatal depression effects on early development: A review. *Infant Behavior & Development* 34:1–14. DOI: 10.1016/j.infbeh.2010.09.008

The article reviews literature on prenatal and postnatal depression and influences on fetal, infant, and child outcomes. The need for research to address the knowledge gap and the methodological complexities that influence the findings from the studies reviewed are discussed. Available online for purchase or by subscription.

Kinsella, Michael T., and Catherine Monk. 2009. Impact of maternal stress, depression, and anxiety on fetal neurobehavioral development. *Clinical Obstetrics & Gynecology* 52:425–440. DOI: 10.1097/GRF.ob013e3181b52df1

This review of the literature is relevant to the fetal programming hypothesis in finding that exposure in utero to the influence of maternal psychological states can have long-term effects across the lifespan. A detailed table is provided that summarizes the studies reviewed. Clinical implications are described. Available online for purchase or by subscription.

Pearson, R. M., R. Melotti, J. Heron, et al. 2012. Disruption to the development of maternal responsiveness? The impact of prenatal depression on mother–infant interactions. *Infant Behavior & Development* 35:613–626. DOI: 10.1016/j.infbeh.2012.07.020

This empirical study investigates the influence of prenatal and postnatal maternal depression and infant outcomes and the possible mediating influence of depression in reducing maternal responsiveness. Timing of depression influenced the outcomes. The importance of interventions of facilitate maternal responsiveness in depressed women who are pregnant is discussed. Available online for purchase or by subscription.

van Batenburg-Eddes, Tamara, Laila de Groot, Anja C. Huizink, et al. 2009. Maternal symptoms of anxiety during pregnancy affect infant neuromotor development: The generation R study. *Developmental Neuropsychology* 34:476–493. DOI: 10.1080/87565640902964508

This empirical study investigates the impacts of maternal depression and anxiety during and after pregnancy and infants' neuromotor development at 3 months. High prenatal maternal anxiety and depression impacted infant outcomes. Available online for purchase or by subscription.

Wojcicki, Janet M., Katherine Holbrook, Robert H. Lustig, et al. 2011. Chronic maternal depression is associated with reduced weight gain in Latino infants from birth to 2 years of age. *PloS One* 6.2: e16737.

Prenatal and postnatal depressive symptoms experienced during pregnancy were examined in relation to growth in Latino infants aged birth to 2 years. Depression during the prenatal and postnatal periods was associated with reduced weight gain in Latino infants and failure to thrive.

EXPOSURE TO MATERNAL STRESS AND DISTRESS

A large body of research has shown that prenatal exposure to maternal stress influences fetal as well as infant postnatal development. The types of stress mothers experience during pregnancy vary from daily hassles to traumatic events. Class, et al. 2011 and Davis and Sandman 2010 explore the timing of stress exposure as determinants of fetal growth and infant outcomes. Kinney, et al. 2008 reviews the impact of prenatal environmental stress and autism. Kingston, et al. 2012 uses a broader construct, “distress,” that combines stress with other mental health problems to study impacts on infant outcomes. Mulder, et al. 2002 includes both human and animal studies in a review of maternal stress exposure and fetal and birth outcomes. Zhu, et al. 2010 reports finding lower birth weights in infants born to mothers experiencing stress resulting from severe life events. Mackey, et al. 2000 and Rondo, et al. 2003 report findings from studies of exposure of women to multiple stress sources on labor, fetal growth, and birth outcomes.

Class, Quetzal A., Paul Lichtenstein, Niklas Långström, and Brian M. D’Onofrio. 2011. Timing of prenatal maternal exposure to severe life events and adverse pregnancy outcomes: A population study of 2.6 million pregnancies. *Psychosomatic Medicine* 73.3: 234–241. DOI: 10.1097/PSY.ob013e31820a62ce

This investigates the effects of stress exposure and timing on gestational age, preterm birth, birth weight, and size for gestational age. Greatest impacts were noted during

the second trimester, particularly months 5 and 6. There are implications for a fetal programming hypothesis.

Davis, Elysia, and Curt A. Sandman. 2010. The timing of prenatal exposure to maternal cortisol and psychological stress is associated with human infant cognitive development. *Child Development* 81.1: 131–148. DOI: 10.1111/j.1467-8624.2009.01385.x

This empirical study investigates timing of exposure to pregnancy-specific anxiety and elevated levels of maternal cortisol, with early versus late exposure having opposite effects on the cognitive performance of infants at 12 months of age. Presumed fetal programming effects based on cognitive performance in infancy are discussed. Available online for purchase or by subscription.

Kingston, Dawn, Suzanne Tough, and Heather Whitfield. 2012. Prenatal and postpartum maternal psychological distress and infant development: A systematic review. *Child Psychiatry and Human Development* 43:683–714. DOI: 10.1007/s10578-012-0291-4

This is a review of research on prenatal and postnatal maternal psychological distress and infant outcomes. Prenatal maternal distress influences cognitive, behavioral, and psychomotor outcomes, postnatal maternal distress influences socio-emotional and cognitive outcomes. Discussions on research, clinical, and policy implications are included. Details on reviewed studies are in tables. Available online for purchase or by subscription.

Kinney, Dennis K., Kerim M. Munir, David J. Crowley, and Andrea M. Miller. 2008. Prenatal stress and risk for autism. *Neuroscience Biobehavior Review* 32:1519–1532. DOI: 10.1016/j.neubiorev.2008.06.004

This article is a comprehensive review of effects of prenatal exposure to environmental stress on autism as well as other postnatal abnormalities. Studies reviewed include a variety of methods and participants (human and animal). Evidence of links between prenatal stress and autism is provided. The findings have possible implications for prevention and treatment. Available online for purchase or by subscription.

Mackey, Marlene C., Carol A. Williams, and Cecilia M. Tiller. 2000. Stress, pre-term labour, and birth outcomes. *Journal of Advanced Nursing* 32.3: 666–674. DOI: 10.1046/j.1365-2648.2000.01526.x

The impacts of stress (daily hassles and mood) on birth outcomes were studied in matched groups of black women and white women, with and without preterm labor. Stress measures were not related to preterm labor, preterm birth, or birth weight, but differences within the preterm labor group were found for stress and impacts on birth outcomes. Available online for purchase or by subscription.

Mulder, E. J. H., P. G. Robles de Medina, A. C. Huizink, B. R. H. Van den Bergh, J. K. Buitelaar, and G. H. A. Visser. 2002. Prenatal maternal stress: Effects on pregnancy and the (unborn) child. *Early Human Development* 70:3–14. DOI: 10.1016/S0378-3782(02)00075-0

The article reviews animal and human research studies on maternal stress and its consequences on pregnancy, fetal development, and birth outcomes. A graphic detailing these relations is provided. Possible intervention approaches to reducing prenatal maternal stress and the need for increased awareness of the importance of stress regulation are discussed. Available online for purchase or by subscription.

Rondo, Patricia H. C., Renato F. Ferreira, Fabiane Nogueira, M. C. N. Ribeiro, H. Lobert, and Rinaldo Artes. 2003. Maternal psychological stress and distress as predictors of low birth weight, prematurity and intrauterine growth retardation. *European Journal of Clinical Nutrition* 57.2: 266–272. DOI: 10.1038/sj.ejcn.1601526

This prospective study investigates impacts of maternal stress, distress, and anxiety on pregnancy outcomes. Distress, but not stress or anxiety, was related to birth weight and prematurity at some trimester points, but not to intrauterine growth retardation. Some obstetric risks (alone or with distress) predicted outcomes.

Zhu, Peng, Fangbiao Tao, Jiahua Hao, Ying Sun, and Xiaomin Jiang. 2010. Prenatal life events stress: Implications for preterm birth and infant birthweight. *American Journal of Obstetrics and Gynecology* 203.1: 34.e1–34.e8.

Exposure to severe life events stress was defined using cut scores on a questionnaire asking about events and perceptions of events. The prospective study found that trimester of exposure to severe life events influenced preterm birth and birth weight outcomes. Other assessed covariates were not systematically related to outcomes. Available online for purchase or by subscription.

EXPOSURE TO MATERNAL WEIGHT GAIN AND OBESITY

Maternal weight gain is common during pregnancy, but excessive weight gain can be associated with adverse infant outcomes. Research evidence on effects of weight gain as well as maternal obesity is important to understanding the bases of concerns about impacts on weight in infancy and childhood and future health status. Farah, et al. 2011 examines the timing of maternal weight gain and maternal body composition in influencing infant birth weight. Hull, et al. 2008 and Sewell, et al. 2006 examine how normal and overweight/obese body mass index (BMI) of mothers influenced that of their infants. Hull, et al. 2011 finds that obesity, even in women with appropriate gestational

weight gain (GWG), resulted in infants with more body fat and fat mass. Josefson, et al. 2013 finds excessive GWG in women with normal prepregnancy weight resulted in the birth of infants with more fat mass and body fat. Modi, et al. 2011 studies relations between increases in maternal BMI and infant adiposity. Ode, et al. 2012 reports on the decelerated growth in infants at 3 months who had been born to overweight or obese mothers. Stothard, et al. 2009 reviews evidence of relations between maternal overweight or obesity and risks for fetal anomalies.

Farah, Nadine, Bernard Stuart, Valerie Donnelly, Mairead M. Kennelly, and Michael J. Turner. 2011. The influence of maternal body composition on birth weight. *European Journal of Obstetrics & Gynecology and Reproductive Biology* 157.1: 14–17. DOI: 10.1016/j.ejogrb.2010.12.047

Measures of maternal body composition at each trimester were examined for impact on birth weight. Gestational weight gain before the third trimester, but not early pregnancy weight gain, influenced infant birth weight. Details on specific measures of maternal body composition are informative. Available online for purchase or by subscription.

Hull, Holly R., Mary K. Dinger, Allen W. Knehans, David M. Thompson, and David A. Fields. 2008. Impact of maternal body mass index on neonate birthweight and body composition. *American Journal of Obstetrics and Gynecology* 198.4: 416.e1– 416.e5.

The study examined body weight and composition (percent fat, fat mass, and fat-free mass) of infants born to women with prepregnancy normal or overweight/obese BMI. Infants of normal BMI mothers had less percent fat and fat mass and less fat free mass but no differences in birth weight were found. Available online for purchase or by subscription.

Hull, Holly R., John C. Thornton, Yin Ji, et al. 2011. Higher infant body fat with excessive gestational weight gain in overweight women. *American Journal of Obstetrics and Gynecology* 205.3: 211.e1–211.e7.

Groups were identified by prepregnancy BMI (normal, overweight, obese) and gestational weight gain (GWG: appropriate/excessive). Higher percent fat and fat mass was associated with obesity in both GWG groups. Infants of normal and overweight women with appropriate GWG had less percent fat and fat mass. Optimal intervention times for overweight and obese women are discussed. Available online for purchase or by subscription.

Josefson, Jami L., Joseph A. Hoffmann, and Boyd E. Metzger. 2013. Excessive weight gain in women with a normal prepregnancy BMI is associated with increased

neonatal adiposity. *Pediatric Obesity*. DOI: 10.1111/j.2047-6310.2012.00132.x

This is an empirical study of gestational weight gain (GWG) in women with normal prepregnancy BMI. Infants of women with excessive GWG had more fat mass and body fat, indicators of adiposity linked with risk of obesity. Timing of participants' excessive weight gain was not known. Available online for purchase or by subscription.

Modi, Neena, Dominika Murgasova, Rikke Ruager-Martin, et al. 2011. The influence of maternal body mass index on infant adiposity and hepatic lipid content. *Pediatric Research* 70.3: 287–291. DOI: 10.1203/PDR.obo13e318225f9b1

Unit increases in maternal BMI of women with normal BMI were examined for impacts on newborn adipose tissue content and distribution and liver lipid. The authors discuss evidence needed to establish whether the found relations index life-long trajectories of health consequences.

Ode, Katie Larson, Heather L. Gray, Sara E. Ramel, Michael K. Georgieff, and Ellen W. Demerath. 2012. Decelerated early growth in infants of overweight and obese mothers. *Journal of Pediatrics* 161.6: 1028–1034. DOI: 10.1016/j.jpeds.2012.06.001

This prospective study investigates maternal prepregnancy BMI and infant outcomes (weight, length, fat-free mass, and fat mass) at 2 weeks and 3 months. At 3 months (but not 2 weeks), infants of overweight or obese mothers showed decelerations in gains. Breastfeeding did not influence the results, and smoking data were not available. Available online for purchase or by subscription.

Sewell, Mark F., Lorraine Huston-Presley, Dennis M. Super, and Patrick Catalano. 2006. Increased neonatal fat mass, not lean body mass, is associated with maternal obesity. *American Journal of Obstetrics and Gynecology* 195.4: 1100–1103. DOI: 10.1016/j.ajog.2006.06.014

The study examined overweight/obese and lean/normal mothers based on BMI and neonate body composition. Outcomes of infant body composition and weight were measured along with maternal weight. Heavier infants with increased levels of adiposity are born to overweight/obese mothers, which may be risk factors for adolescent obesity metabolic disorder. Available online for purchase or by subscription.

Stothard, Katherine J., Peter W. G. Tennant, Ruth Bell, and Judith Rankin. 2009. Maternal overweight and obesity and the risk of congenital anomalies: A systematic review and meta-analysis. *Journal of the American Medical Association* 301.6: 636–650. DOI: 10.1001/jama.2009.113

This review focuses on the impacts of maternal weight and fetal anomalies (e.g., neural tube defects, cardiovascular anomalies, cleft palate, limb anomalies). Many of the hypothesized associations are confirmed. Detailed information is provided on article selection and meta-analysis methods, study findings for each fetal anomaly, and sensitivity analyses.

Influence of Prenatal Attachment

Attachment refers to the emotional bond between mother, father, or caregiver and child. Maternal-infant attachment begins in the prenatal period based on interactions between mother and fetus in the womb and is influenced by a myriad of variables, including fetal movement, information from medical imaging, and maternal hormonal change. Technological advances (such as the ultrasound) have changed the way that a woman experiences this relationship. The articles in this section address attachment before birth. Prenatal and postnatal attachment is not the same construct, and do not use the same measures. However, there is general agreement that both are strongly related to child outcomes and that prenatal attachment is an antecedent of postnatal attachment. Fetal attachment refers to a mother's feeling toward her fetus, and recent literature emphasizes the transactional nature of the relationship. Alhusen 2008 provides a detailed review of the breadth of literature on maternal and fetal attachment. Brandon, et al. 2009 includes maternal and paternal attachment research in a review of attachment theory and research. Cannella 2005 identifies correlated and uncorrelated relations between attachment and psychosocial, demographic, and pregnancy outcomes. Condon, et al. 2013 focuses on paternal attachment in a longitudinal study of prenatal and postnatal attachment. Laxton-Kane and Slade 2002 relates prenatal attachment to the pregnancy experience and infant care. Perry, et al. 2011 examines attachment quality of mothers with depression. Shin, et al. 2006 explores relations between mother-fetal and mother-infant attachment quality. Yarcheski, et al. 2009 reports results of a meta-analysis of predictors of attachment.

Alhusen, Jeanne L. 2008. A literature update on maternal-fetal attachment. *Journal of Obstetric, Gynecologic, & Neonatal Nursing* 37.3: 315–328. DOI: 10.1111/j.1552-6909.2008.00241.x

This article reviews 22 studies, published since 2000, exploring factors that influence maternal-fetal attachment. The review defines and reports study findings on the roles of technology and diagnostics, demographics, mood states, and risk or perceived risk factors. The section “clinical implications and future directions” provides information on research knowledge gaps. Available online for purchase or by subscription.

Brandon, Anna R., Sandra Pitts, Wayne H. Denton, C. Allen Stringer, and H. M. Evans. 2009. A history of the theory of prenatal attachment. *Journal of Prenatal & Perinatal Psychology & Health* 23.4: 201–222.

This article reviews Bowlby's theory of attachment and attachment theory research. Prenatal attachment theory and construct measurement studies are described, along with reviews of published critiques and studies of the relevance of prenatal attachment to infant outcomes. Research on paternal attachment is also reviewed. A

Cannella, Barbara L. 2005. Maternal-fetal attachment: An integrative review. *Journal of Advanced Nursing* 50.1: 60–68. DOI: 10.1111/j.1365-2648.2004.03349.x

This review focuses on 41 studies of mother-fetal attachment. While some significant correlations are reported, many relations are not significant. The author describes some short-comings of existing research along with recommendations for needed research. Available online for purchase or by subscription.

Condon, John, Carolyn Corkindale, Philip Boyce, and Elizabeth Gamble. 2013. A longitudinal study of father-to-infant attachment: Antecedents and correlates. *Journal of Reproductive and Infant Psychology* 31.1: 15–30. DOI: 10.1080/02646838.2012.757694

This empirical study examines father's prenatal and postnatal attachment to their infants. A continuity of attachment is documented using self-report measures, along with measures of some partner characteristics and father emotional well being. Prenatal attachment measures are more strongly related than postnatal attachment. Clinical implications of the findings are discussed. Available online for purchase or by subscription.

Laxton-Kane, Martha, and Pauline Slade. 2002. The role of maternal prenatal attachment in a woman's experience of pregnancy and implications for the process of care. *Journal of Reproductive and Infant Psychology* 20.4: 253–266. DOI: 10.1080/0264683021000033174

This review article examines a variety of factors to determine evidence of impacts on maternal-fetal attachment. Factors examined include demographics, pregnancy risk, prenatal care, psychological factors, and social supports. Implications for attachment of low levels of prenatal attachment and maternal behaviors with known negative impacts on fetal development are described. Available online for purchase or by subscription.

Perry, Deborah F., Anna K. Ettinger, Tamar Mendelson, and Huynh-Nhu Le. 2011. Prenatal depression predicts postpartum maternal attachment in low-income Latina mothers with infants. *Infant Behavior and Development* 34.2: 339–350. DOI: 10.1016/j.infbeh.2011.02.005

This empirical study examines variations in postnatal attachment quality in a sample of mothers enrolled a prenatal depression prevention trial. Quality of attachment is related to depressive symptoms in late pregnancy, and pregnancy intention. Applications to intervention with women who are depressed or at risk are discussed. Available online for purchase or by subscription.

Shin, Hyunjeong, Young-Joo Park, and Mi Ja Kim. 2006. Predictors of maternal sensitivity during the early postpartum period. *Journal of Advanced Nursing* 55.4: 425–434. DOI: 10.1111/j.1365-2648.2006.03943.x

This empirical study of Korean mothers examines prenatal factors affecting maternal attachment within 6 weeks of birth. Among the significant predictors is maternal-fetal attachment. Maternal identify and social support are also associated with attachment. Available online for purchase or by subscription.

Yarcheski, Adela, Noreen E. Mahon, Thomas J. Yarcheski, Michele M. Hanks, and Barbara L. Cannella. 2009. A meta-analytic study of predictors of maternal-fetal attachment. *International Journal of Nursing Studies* 46.5: 708–715. DOI: 10.1016/j.ijnurstu.2008.10.013

This meta-analysis of 72 studies examined relations between 14 predictors and maternal-fetal attachment. Moderate predictors included social support and prenatal testing, 10 low predictors included anxiety, self-esteem, depression, age, parity, marital status, education and high-risk pregnancy was a “trivial” predictor. The findings are related to research knowledge gaps and practice. Available online for purchase or by subscription.

Moderators of Prenatal Development

A simple but common research design is one that explores direct relations between an independent variable, such as prenatal exposure of a fetus to an auditory stimulus, and a dependent variable, such as infant habituation to the auditory stimulus. However, more complex designs can be created to explore the role of moderating variables to determine if findings exploring direct relations between variables change when moderating variables are considered. In this section, some examples of recent publications report the influence of moderating variables in study outcomes. Two studies investigate attachment

or parenting quality as moderators. Bergman, et al. 2010 investigates mother-infant attachment as a moderator of prenatal maternal anxiety/stress and infant outcomes, while Hayes, et al. 2013 investigates parenting quality as a moderator of maternal depression and infant behavior. Bouchard 2011 explores socialenvironmental variables as moderator of the quality of prenatal attachment. Buchmayer, et al. 2009 explores the moderating roles of obstetric and neonatal complications on associations between preterm birth and autism risk. DiPietro 2010 includes psychological and psychophysiological variables in considering mother-fetal attachment. Grote, et al. 2010 explores social variables as moderators of maternal depression and infant outcomes. Schuetze, et al. 2006 finds that maternal anxiety moderated links between cocaine and sleep problems.

Bergman, Kristin, Pampa Sarkar, Vivette Glover, and Thomas G. O'Connor. 2010. Maternal prenatal cortisol and infant cognitive development: Moderation by infant-mother attachment. *Biological Psychiatry* 67.11: 1026–1032. DOI: 10.1016/j.biopsych.2010.01.002

This study sought to extend findings from animal studies to humans by investigating the role of mother-infant attachment as a moderator of maternal anxiety/stress on infant cognitive development. Findings of relations between prenatal cortisol level and cognitive impairment was moderated by quality of the mother-infant relationship. Available online for purchase or by subscription.

Bouchard, Geneviève. 2011. The role of psychosocial variables in prenatal attachment: An examination of moderational effects. *Journal of Reproductive and Infant Psychology* 29.3: 197–207. DOI: 10.1080/02646838.2011.592975

This article examines interactions in the mother's psychosocial environment (prenatal attachment, neuroticism, marital quality, attachment to parents, and pregnancy planning) to show associations of risk and protective factors on prenatal attachment. Psychosocial variables influencing fathers' prenatal attachment are included. Available online for purchase or by subscription.

Buchmayer, Susanne, Stefan Johansson, Anna Johansson, Christina M. Hultman, Par Sparén, and Sven Cnattingius. 2009. Can association between preterm birth and autism be explained by maternal or neonatal morbidity?. *Pediatrics* 124.5: e817– e825.

This empirical, retrospective study investigates links between prematurity and autism. Risk of autism is higher in preterm infants, but risk is moderated by obstetric and neonatal conditions. Complications influencing brain development increase autism risk. Better understanding of autism risk factors for children born preterm and at term is needed.

DiPietro, Janet A. 2010. Psychological and psychophysiological considerations regarding the maternal–fetal relationship. *Infant And Child Development* 19.1: 27–38. DOI: 10.1002/icd.651

This theoretical article examines relations between maternal psychological state, responsiveness and psychophysiological functioning, and fetal response in an effort to better understand maternal-fetal attachment. The roles of different moderators are discussed. Available online for purchase or by subscription.

Grote, Nancy K., Jeffrey A. Bridge, Amelia R. Gavin, Jennifer L. Melville, Satish Iyengar, and Wayne J. Katon. 2010. A metaanalysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Archives of General Psychiatry* 67.10: 1012–1024. DOI: 10.1001/archgenpsychiatry.2010.111

This is a meta-analysis targeting studies of prenatal maternal depression and risks of preterm birth, low birth weight, and intrauterine grow restriction. Predicted associations of depression and preterm birth and low birth weight outcomes are identified, but country location and SES moderate outcomes. The importance of screening for depression is discussed.

Hayes, Lisa J., Sherryl H. Goodman, and Elizabeth Carlson. 2013. Maternal antenatal depression and infant disorganized attachment at 12 months. *Attachment & Human Development* 15.2: 133–153. DOI: 10.1080/14616734.2013.743256

This study examines the influence of maternal prenatal and postnatal depression, parenting quality, and infant attachment. Parenting quality is found to moderate the link between depression and infant attachment quality. Targeting parenting behaviors could be a fruitful approach for interventions. Available online for purchase or by subscription.

Schuetze, Pamela, Desirae Lawton, and Rina Eiden. 2006. Prenatal cocaine exposure and infant sleep at 7 months of age: The influence of the caregiving environment. *Infant Mental Health* 27.4: 383–404. DOI: 10.1002/imhj.20097

An empirical study examining the relationship between prenatal cocaine exposure and infant sleep problems at 7 months of age. Infants exposed to cocaine in utero have more severe sleep problems. Maternal anxiety positively moderates links between cocaine and sleep problems. Cocaine-exposed infants in nonparental care had less severe sleep problems. Available online for purchase or by subscription.